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THE
TREATMENT OF DIPHTHERIA
WITH
DIPHTHERIA ANTITOXIN.

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To Robert Koch and his associates is the honor due for laying the foundation that led to the discoveries of the various pathogenic micro-organisms—tuberculosis, typhus, diphtheria, cholera, etc. In his work (*Untersuchungsmethoden von pathogenen Organismen*) Koch gave an impetus to the study of bacteriology, which at the present time is the common property of the scientific world. The etiology of diseases was investigated; the results of these investigations demonstrated and proven. The diagnosis of diseases was by the means of bacteriology rendered easy and certain, and now the realms of the therapeutists have been invaded and the bacteriologists give to the clinician new remedies and new methods. This transition is the natural sequence of the present doctrines concerning the infectious diseases.

When the causes of diseases were proven, then came the study of a preventative, and thus was laid the groundwork for a rational prophylaxis. The discovery of tuberculin by Koch may be called the foundation-stone upon which all the later discoveries have been laid and which has led to that newest method—the serum-therapy of Behring and others.

Loeffler (a student of Koch) was the first to isolate and cultivate the micro-organism of diphtheria which had been previously discovered by Klebs and bears the name of Klebs-Loeffler. Discovered in 1884; small, slightly-curved rods about as long as the tubercle bacilli and twice as broad, possessing no movement; do not liquefy gelatin; are not very resistant, being destroyed by a temperature of 50° C., but they have lived in blood-serum five months; grow readily on all media between temperatures of 20° and 40° C.



They are facultative anaërobic, and grow quite rapidly and profusely and may be cultivated on gelatin plates, glycerin agar-agar (stab-culture), potato (on alkaline surface—a grayish layer in forty-eight hours), and in blood-serum (after Loeffler). “Blood-serum 3, bouillon 1; the bouillon contains peptone 1 per cent., chloride of sodium $\frac{1}{2}$ per cent., and dextrine 1 per cent.” Is not colored by Gram’s method; stained best with Loeffler’s alkaline methylene-blue (M. V. Ball.—*Bacteriology*).

Loeffler, as well as Roux and Yersin and Sydney Martin, have further investigated the disease. Their experiments have proven that it is not the mere presence of the bacilli that gives rise to all the symptoms we meet with, but their products; that is, the ptomaines or poisonous substances produced by it.

Roux and Yersin substantiated their theory by separating the bacillus from the ptomaines, and subjecting it to chemic analysis and physiologic test. They described the disease as a toxæmia differing from others in the respect that the toxin acts as a ferment, which when injected into living tissues even in the most minute quantities ushered into existence certain well-defined albuminous substances or bodies. These albuminoids were isolated by Sydney Martin from various organs obtained from persons who died from diphtheria. The substance when secured was subjected to alcohol and resolved itself into a proto- and dextro-albumose, which he injected into rabbits. In doses of 0.117 per kilo it produced a febrile condition and œdema in the animal; slightly increasing the amount to 0.112 per kilo rapid death of the animal followed. Intravenous injections produced fever, progressive paralysis, and degeneration of the heart, nerves, and muscles precisely analogous to those conditions resulting from diphtheria.

Brieger and Fränkel, as well as Proskauer and Wasserman, busied themselves with the further chemistry of the disease. Brieger and Fränkel, through frequent precipitation of the culture-bouillon with acetic acid and alcohol, obtained a white amorphous body which gave all the reactions of an albumin. It is soluble in water, and decomposes by high temperature.

These “toxins,” as well as “antitoxins” or substances that establish immunity to specific diseases in animals, have been shown by Buchner to be probably the direct products of bacterial cells.

These results, on the investigation of the products, gave rise to further experiments, and Roux, in France, Brieger and Fränkel and Behring, in Germany, pursued the same studies leading to immunization.

Brieger and Fränkel, by injecting 10 to 20 c.cm. of a three-weeks' old culture of diphtheria bacilli which had been heated to 70° C. for one hour, produced an immunity in guinea-pigs against the virulent form.

Behring found several ways to make animals immune. One method was to inject them with diphtheria and then inject trichloriodine into them, which prevented them from dying, and they were then immune.

The immunity of individuals against disease is understood to depend upon the destruction, by certain agents, of the supposed living cause of the disease. These agents may also act by hindering the growth of the living cause or by destroying its infectious properties by the destruction of the poisonous material produced in the infected organism, or by imparting a higher resisting power against this poisonous material.

Behring's serum-therapy is based upon these ideas and depends upon his own discovered fact: that we can through subcutaneous injections of the blood of animals which are rendered immune from certain bacteria render other animals immune against inoculation of the same bacteria; and not only does such an injection (*impfung*) protect the animal against living bacteria, but against their "toxins," as has been pointed out by Behring and Kitasato for tetanus bacilli and tetanus toxins.

This discovery of Behring's is the beginning of a new epoch in the science of immunization. Until this period immunization could only be obtained by giving the animal attenuated bacteria cultures, or solutions of cultures freed from living organism. Pasteur's methods of immunization against hydrophobia and anthrax depend upon the results of these experiments, immunization being obtained by having the individual go through a weaker or modified form of the disease, similar also to vaccination against variola with cowpock (vaccine virus). The result of passing through a milder form of disease is to protect the individual against an infection of a more virulent matter, as vaccinia modifies variola, with the result, if there be infection, varioloid.

Behring's method is entirely different; where formerly a disease was produced to protect from a more virulent disease, now is injected into the organism a substance, harmless in itself, which protects the individual not only against infection, but, if already infected, from its results. To this he has given the name "antitoxin," asserting that another name, "gegengift"—against poison—might lead one to

the belief that the antitoxin was in its name and nature a poison, a fallacy which he emphatically desires to be known (*Das neue Diphtheriemittel*, Behring, 1894, page 10).

It is, therefore, an entirely different process of immunization from Pasteur's.

In Pasteur's method every individual receives a special virus for a special case to develop immunization. In Behring's method the one virus (serum), if it has immunization powers, is capable of transmitting immunization to a whole series of cases. This has been proven in diphtheria and tetanus.

Ehlich proposes the names "active and passive immunization," to distinguish those that have been immunized with serum and those with the cultures or the disease. In the latter, the passive immunization is not lasting, because the individual has had no work put upon the cells to become immune, but has received the ready-made serum; as long as it is in the blood, so long is there immunization. In the active form the individual has obtained immunization by labor obtained through the activity of its own cells. He holds this property longer. To substantiate this theory he gives as examples those individuals who have passed through an infectious disease, become immuned, and retain immunization throughout life. I give as examples of his theory, vaccinia against variola—where varioloid may result—for the passive; scarlatina against a reinfection for the active immunization.

The antitoxin, or "gegengift," which, to the blood of immunized individuals, gives that specific protection, acts specifically, so that tetanus antitoxin protects only against tetanus or diphtheria antitoxin against diphtheria.

Diphtheria antitoxin serum is obtained from the blood of animals rendered immune to the disease by the prolonged injection of minute, but gradually increasing quantities of diphtheria "toxin," a fluid obtained by the cultivation of the diphtheritic bacilli in nutrient broth (*Blutserumtherapie und Geschichte der Diphtherie*, Behring).

The principles of Behring's method is followed by Roux and Aronson, as well as those who are making it in this country.

Of the precise method of obtaining the diphtheria serum: "The method first employed by Behring for the immunization of animals and consequent production of 'antitoxin' in their blood was one by which the animals were immunized to the activities of the bacillus and able to resist its growth in the body. For this purpose, dogs,

goats, and smaller animals were injected first with cultures of diphtheria, containing only the dead bodies of bacilli killed by heat. When these could be tolerated without any considerable local irritation, living cultures attenuated by heat were introduced to pave the way for virulent organisms, which were withheld until the vital resistance acquired was sufficient to prevent them from causing death. In this way Behring was able to produce immunity in animals ordinarily susceptible to the disease, and to discover in their blood a substance, which, when secured in solution in clear serum, and introduced into animals suffering from the disease, seemed potent to neutralize the diphtheria poison and enable the animals to recover. Behring, however, foresaw that the chief source of danger in the infection was the toxic product of the bacillus, not the bacillus itself, and that a stronger serum—*i. e.*, one possessed of more of the antitoxic substance—was required to save the lives of animals into which the toxin was injected, than to save those inoculated with living bacilli.

“In the incubator in his laboratory Behring had a flask of bouillon which, having been inoculated with diphtheria bacilli, had been allowed to remain undisturbed for two years. From it every living bacillus had disappeared, the nutrient having been exhausted. Repeated experiments showed the culture absolutely sterile, yet so great were its toxic powers that 0.1 c.cm. injected into a 500-gramme guinea-pig would cause death in twenty-four hours.

“This prodigiously powerful poison was that used in the antitoxin experiments, and all Behring’s energies were devoted to the production of a neutralizing substance so strong that a small quantity of it would suffice to neutralize a large quantity of the poison. So successful was Behring in his experimentation as to be able to produce an almost incredible amount of protection for guinea-pigs, both against inoculation with living bacilli and injection of the poison.” (Diphtheria Antitoxic Serum, H. K. Mulford Co.) In this city Diphtheria Antitoxic Serum is manufactured by the H. K. Mulford Co., under the direction of Dr. Joseph McFarland, Lecturer on Bacteriology in the Medical Department of the University of Pennsylvania. Their bacteriological laboratory has been fully equipped for this purpose, and is situated near Fairmount Park. I have been enabled to visit this laboratory, and Dr. McFarland very kindly showed me the entire work of this establishment. The horses used for his purpose were under the supervision of Dr. Leonard Pearson, Professor of Theory and Practice of Veterinary Medicine in the

University of Pennsylvania. The products were not only standardized in the laboratory, but also by the Department of Hygiene in the University of Pennsylvania.

For the manufacture of the antitoxin, Dr. McFarland pursues Roux's method. This depends upon the continuous and progressive introduction of a very powerful toxin into a non-susceptible animal, and the production, in this animal, of the antitoxin, by the stimulated cells of the tissues and blood. This method is pursued by him as follows: From numerous cultures of the *bacillus diphtheriae* a particular virulent one is chosen. To be very virulent $\frac{1}{2}$ c.cm. of a twenty-four-hour-old bouillon culture should kill a 500-gramme guinea-pig in from twenty-four to thirty-six hours. With this bacillus a large flask of alkaline, 2 per cent. peptone bouillon, is inoculated and placed in the incubator. At the end of twenty-four to forty-eight hours about 40 c.cm. of this culture are added to each of a number of very wide, flat flasks, with long necks and a tubulature at the side (Fernbach flasks), each containing about one litre of similar bouillon.

These flasks after being inoculated are also placed in the incubator for twenty-four hours, until the growth be well established, after which the cotton plugs, which have closed the mouth and tubulature, are pushed well down the tubes, rubber corks containing a glass tube inserted above the cotton, and the tubes connected with an aspirating apparatus, by which a current of air is kept passing through the flasks from mouth to tubulature.

The object of this seems to be twofold. Fernbach, the inventor of the method, observed that the liberation of metabolic products of micro-organisms keeps pace with their vegetation, and is at its maximum when the bacilli are multiplying and dying with great rapidity, the death of each organism seeming to liberate the poison which its protoplasm contained. The primary object of the Fernbach flask was to supply the appropriate conditions for rapid vegetation by a current of fresh air. It can be readily observed that from massive cultures of diphtheria, in liquid media, especially a pungent odor arises. The second function of the current of air is to remove this effluvium. In order not to dry up the culture medium, the air passing through the flasks is first made to pass through a wash-bottle, contaminating micro-organisms being excluded by the cotton-plugs in the neck of the flasks and in the tubulature. The flasks thus arranged are kept in an incubator at a temperature of 32° C. for three to four

weeks, after which the toxin supposed to be virulent is filtered and tested. The filtration of the toxins is a matter requiring considerable care as regards the filtrate, which, although devoid of bacilli when passed through the filter, is as good a culture medium for bacteria other than the diphtheria bacillus as ever. The filter used is the Chamberland. The strength of the toxin is estimated by injecting into guinea-pigs, the desired strength being sufficient for 0.1 c.cm. to kill a 500-gramme animal in twenty-four hours.

If the filtered toxin be of the desired strength it can at once be used. If, however, as is the case in a great number of instances, the toxin prove weak, it should be rejected.

The animal employed is the horse. Before beginning the treatment, it must be tested for tuberculosis and glanders with tuberculin and mallein. Much individual variation occurs among horses in their susceptibility to the action of the toxins, hence it is always well to begin the administration with a very small amount. Roux begins with 0.5 c.cm., and repeats the injection about every eight days, according to the condition of the animal, doubling the amount as often as possible, and as rapidly as possible ascending to the enormous amount of 200 to 250 c.cm.

The condition of the horse during all this time must be carefully watched and estimated. The injection generally causes fever, which cannot be borne too long without danger. The appetite must be carefully noted. The animals should be weighed at rather frequent intervals. All these precautions are necessary to keep the horses from falling into a condition of cachexia, from which they recover with difficulty, if at all, and in which they can yield no antitoxin, because the blood is saturated with toxin, not antitoxin.

When the treatment has been kept up for three or four months, and the animals have reached the point at which they can stand the injection of 200–250 c.cm. without other general or local symptoms than a large oedema at the point of injection, they are about ready to furnish antitoxin of value.

A trocar, with a canula attached to a rubber-tube, is passed into the jugular vein of the animal, and the blood allowed to flow through the tube into sterile glass jars prepared to receive it.

The jars are stood upon ice, after the blood coagulates, for two days or more, until the serum separates. The clear serum is withdrawn by the pipette and placed in sterile receptacles.

As with the toxins, so with the antitoxins, disappointment is liable

to meet the experiment at the last moment. All the horses will not furnish the same degree of antitoxicity in their serum, and the test, which must be performed upon guinea-pigs, will sometimes show that the serum from the horse, most carefully treated, is entirely devoid of antitoxic power.

If properly carried out, without haste, the horse being kept in good condition, the power of the serum should be sufficient in an almost infinitesimal amount to protect a guinea-pig against the ordinary fatal dose of diphtheria toxin. The exact value of the serum obtained by Roux's method, to make it equal the accepted standard, is that one part of it shall protect against ten times as many parts of the standard toxin. Thus, if 0.1 c.cm. of the toxin will kill a 500-gramme guinea-pig, 0.01 c.cm. of the antitoxic serum should cause the animal to recover. As ordinarily expressed, 1 gramme of the antitoxin will protect 50,000 grammes of guinea-pig against what would ordinarily be a fatal dose.

By injecting the toxin into a vein, and carrying out the immunization for a longer period of time, a stronger antitoxic value—even twice as strong—can be produced. As, however, a severe urticaria follows the injection of this serum into human beings, its use is not so desirable as the weaker serum.

Serum thus obtained may be kept for quite a while before using. To keep it sterile some antiseptic has been added, as carbolic acid, trikresol, camphor, or the like.

The serum does not retain its power indefinitely, but gradually loses it.

Of the method of using the antitoxin :

The antitoxic serum is used as a curative or immunizing agent by subcutaneous injection into the tissues of the body. The parts chosen by myself, and advised by those who have first used it, are in the back between the scapulæ on either side of the vertebral column. Other parts of the body, as the loins, groins, or sides of the chest, have been selected. The parts are thoroughly cleansed by means of alcohol soaked upon sublimate cotton or gauze, and after injection are hermetically sealed with iodoform collodion. For the purpose of making these injections I have used first a horse hypodermic syringe, requiring, however, two injections, as its capacity was but 5 c.cm. Later, I used a Koch 10-c.cm. syringe, and at the present time I am using a hypodermic syringe made for this purpose by the Mulford Company, its capacity being 12 c.cm.

The amount of antitoxin used depends upon the time of making the injection, the age, and body weight of the individual, and the gravity of the disease: also whether for the purpose of immunization or cure. In these methods I have followed the directions of Behring as given in his announcements with every bottle of the antitoxin.

In the first two days of the disease, if the case be one of average severity, I give an injection equivalent to 600 antitoxin normals. No matter what may be the strength of the antitoxin, I fix my dose to suit this equivalent. For the purpose of better understanding this, I may add that whilst the antitoxin as manufactured by Dr. McFarland has a certain strength, *i. e.*, each gramme being equal to 100 antitoxic normals, Behring has antitoxin of three strengths, *i. e.*: 1. Each gramme representing 60 normals; 2. Each gramme representing 100 normals; 3. Each gramme representing 150 normals. Aronson's antitoxin has the same strength as Behring's No. 2, *i. e.*, each gramme representing 100 normals. Roux's antitoxin is equivalent to Behring's No. 2, each gramme representing 100 normals; and another antitoxin, to which I give the name of Dr. J. Solis-Cohen, has the same equivalent as Behring's No. 3. Of Gibier's antitoxin I know very little of its strength but the assertion that it equals Roux's. This, however, cannot be substantiated, for an extremely large quantity (25 c.cm.) is necessary as a curative injection, which if its strength were such would be unnecessary. It would be superfluous to add the directions which come with each variety of antitoxin; it is sufficient to know the strength in antitoxic normals, to know how to apply it. To resume: If the case be seen on the third day, or if at the beginning the infection be such that leads one to believe in the necessity of prompt treatment, as in laryngeal cases or where the lymphatics be involved, I immediately inject 10 c.cm. or the equivalent 1000 antitoxic normals. I then await results. If in six to twelve or even twenty-four hours no change takes place or the symptoms are aggravated, I inject again 1000 antitoxic normals of the serum, and so on until there be an amelioration of the symptoms shown by a decline or pulse-rate and temperature and an improvement in the general condition. I have noticed another sign which is manifested from six to twelve hours even before the pulse and fever decline and which teaches me that I have used sufficient antitoxin, and that is a blood-red line surrounding the diphtheritic patches in the throat, this line so distinct that it shows the demarcation between the healthy and infected mucous membrane. When this is visible my experience has

taught me to expect a very favorable result in the particular case. The quantity of antitoxin administered can increase to enormous dosage; being harmless, no danger can be apprehended. To what quantity it has been used in one single case my statistics will show. My own statistics show that 2000 antitoxic normals were sufficient in the most serious cases.

The question might arise, What is an antitoxic normal? An antitoxic normal or immunity unit is an amount of antitoxic serum required to save a 500-gramme guinea-pig from the minimum fatal dose of diphtheritic toxin. The number of immunity units per c.cm. gives a standard strength of the serum; for instance, $\frac{1}{100}$ c.cm. will protect a 500-gramme guinea-pig, therefore 1 c.cm. would protect 50,000 grammes or 100 guinea-pigs against the minimum fatal dose; 1 c.cm. of antitoxic serum, which protects 50,000 grammes of guinea-pig, contains 100 antitoxic normals or immunity units, and would protect an individual weighing 100 times as much as a guinea-pig (about 120 pounds), if the susceptibility were the same. As the susceptibility might be the same I give an injection, as an immunizing dose, of 100 antitoxic normals (immunity units) to perfectly healthy individuals exposed to the contagion of diphtheria. That this theory is the correct one and my dosage the correct dose, since I have practised this Behring (Meister Lucius and Brüning Höchst a. M.) has placed before the profession another bottle which he terms No. 0, containing 200 antitoxic normals (immunity units) for immunizing purposes. This he terms an immunizing dose, and is sufficient for healthy children and adults. It protects them against exposure, and even if exposed and show evidence (Loeffler bacilli) of such exposure. To protect individuals who may be exposed by coming into the neighborhood of such infection one-half of this quantity, 100 antitoxic normals (immunity units), is sufficient. To further protect individuals who have been immunized Behring orders that the dose be repeated in eight weeks.

The question now arises, Is diphtheria antitoxic serum a cure for diphtheria? For diphtheria pure and simple where there exists no other infection, I am prepared to say yes. Where, however, other infection exists, manifested by other symptoms, demonstrated by other indications, and proven by bacteriological examination, I must modify this reply, and though my success and statistics have been extraordinary, I think it only proper and truthful to say that this is due to a recognition of the other complications, and a prompt and careful

specific treatment of the same. It is, therefore, a very rational explanation of the brilliant results which the early use of antitoxin have given. When used before the diphtheria toxins have so invaded the tissues as to destroy them, antitoxin is a specific. But where the complex symptoms are such (the degenerations of muscles and nerves, or the toxæmia or septicæmia) that life cannot exist, this or any other method of treatment cannot cure. Understanding diphtheria with all the complications that can arise (infection from streptococci, staphylococcus, pneumococcus, etc.) I modify the treatment and pursue the following method:

After injection of the serum, whether the case was one requiring intubation or not, whatever the variety may be, I immediately ordered a purgative to rid the alimentary canal of any infectious bacilli. For this purpose I give calomel, combining it with salol. I give it hourly, in suitable dosage, until characteristic evacuations, when I cease its administration. At the same time, I administer a judicious amount of stimulants and food. If any complication exists which by its presence endangers life, I administer the antitoxin, but I pay no more attention to the diphtheria except the stimulation and treat that symptom. For example, if it be a pneumonia, my whole energies are directed to that, or if it be a nephritis, my whole treatment is directed toward the kidneys. That this is the correct method my recovery of the cases can demonstrate. In one case of pneumonia, in the practice of Dr. Metzler, our treatment was mainly directed to the lung infection, and the result was a cure. The same incident was noted in the practice of Dr. H. H. Freund. In a case of tubal nephritis (acute), seen by Dr. Van Gasken (health inspector of the district), no other remedial agents were employed but those commonly used in such affection. I can, therefore, safely assert that whilst antitoxin is a specific in diphtheria, it is not a cure-all, and if reliance be placed on this remedy alone disappointment will be the rule instead of the exception. That diphtheria antitoxic serum has curative virtues, none who understand the clinical manifestations of the disease should deny; still there are many who by word and pen decry its virtues and give to it credit for nothing, and even go so far as to place to its discredit downright harm. I have gathered as many of these monographs together as I could, to see upon what grounds this antagonism exists. To combat these assertions, I had prepared a list of questions containing also the points upon which the antagonists of antitoxin lay particular stress. These questions I have sent

to as many physicians as I was able, and who I learned have used the serum, with the purpose of coming to an accurate and truthful conclusion. Besides this, I sent the same questions to the hospitals of different cities with a chart asking for statistics, etc. Whilst my colleagues in private practice have been both kind and prompt in their responses, I must regret to say that I will be unable to give the statistics of the different hospitals, for the simple reason that while the questions may be of vital interest to us as private practising physician, a sort of red-tapism protects some of the hospitals from exposing their statistics, and where I really expected some co-operation a lack of consideration or probably other and more valuable duties prevented such a request being granted. However I strove to make this omission good by requesting the Board of Health of three of our large cities for statistics which might answer somewhat my purpose. Mr. Turner, of our Board of Health, kindly referred to Dr. Taylor, who referred me, etc., and consequently I cannot produce Philadelphia statistics; Dr. Roger S. Tracy, Register of Records, New York Board of Health, reported for New York; and Dr. S. H. Durgin, of the Health Department, Boston, Mass., for Boston. The questions I gave to each were precisely the same, and were a request for the returns received in each office of a case of diphtheria, as well as the returns of the deaths, for each month from 1886 until the present month.

[On the following pages will be found exact copies of the New York and Boston reports, arranged in tabulated form.]

REPORT FROM DR. ROGER S. TRACY, REGISTER OF RECORDS OF BOARD OF HEALTH, NEW YORK CITY.

Diphtheria. New York.	1886		1887		1888		1889		1890		1891		1892		1893		1894		1895	
	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.
January
February ¹	945	155	1331	906	1952	218	2387	200	1343	110	1360	90	1555	153	1449	149	2539	286	2627	179
March	.	140	170	170	352	371	208	187	132	117	137	136	140	114	1449	149	2539	210	2627	142
April	.	131	180	180	232	352	208	187	132	117	137	136	140	114	1449	149	2539	210	2627	154
May	818	142	1399	183	2013	162	2653	228	1270	123	1103	116	1299	163	1515	171	2805	214	2727	155
June	.	130	218	218	352	352	164	164	107	107	102	102	87	80	130	130	2805	214	2727	176
July	.	154	154	154	154	154	154	154	37	37	37	37	89	106	138	138	2805	214	2727	153
August	708	104	1337	103	1100	116	973	85	703	66	900	87	809	76	1265	105	1761	139	1386	127
September	.	85	143	143	60	60	62	62	80	80	91	91	80	80	120	120	1761	139	1386	107
October	.	165	161	161	100	100	60	60	104	104	110	110	90	80	120	120	1761	139	1386	121
November	1266	188	187	187	1426	131	1076	67	1094	107	1511	150	991	134	2239	242	2050	163	1386	163
December	.	218	234	234	164	164	117	117	104	141	1511	150	991	134	2239	242	2050	163	1386	107

REPORT FROM DR. S. H. DURGIN, CHAIRMAN BOARD OF HEALTH OF THE HEALTH DEPARTMENT, BOSTON, MASS.

Diphtheria. Boston.	1886		1887		1888		1889		1890		1891		1892		1893		1894		1895	
	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.	Cases reported.	Deaths returned.
January	122	29	128	38	112	35	179	59	203	63	80	16	102	28	152	49	195	61	340	65
February	104	25	93	29	80	23	150	42	180	49	71	18	108	31	114	32	128	46	294	55
March	110	26	96	24	105	37	193	40	156	41	59	13	114	35	116	31	185	56	205	29
April	66	22	101	19	107	43	205	54	164	40	71	17	135	52	70	27	139	42	191	37
May	73	22	75	22	142	63	170	50	144	36	81	24	107	39	86	33	187	58	221	32
June	94	30	68	22	110	37	165	57	114	29	49	16	77	23	111	25	167	43	327	43
July	75	22	63	11	97	29	93	32	73	28	31	6	76	19	88	39	138	41	268	40
August	78	27	40	14	92	27	99	36	69	27	36	8	78	23	102	28	154	60	268	40
September	85	24	53	25	95	31	99	44	75	19	40	11	79	31	89	31	249	76	268	40
October	133	38	112	31	143	51	137	49	96	18	78	27	144	35	194	72	450	109	268	40
November	111	34	100	36	156	51	130	42	75	18	108	41	185	46	160	58	468	126	268	40
December	140	39	130	45	172	53	174	59	117	33	127	35	175	52	183	69	469	99	268	40

¹ Cases reported are only made up by quarters, not months.² Approximate for two months (July and August). August not made up yet; probably 6 or 8 more.

As it would be both cumbersome and tiresome to read these statistics before you, I have curtailed them into percentages and present them in this manner. I have taken the first six months of each year, and have classed the year 1895 the serum year. Whilst these statistics have not realized our expectation as to show an extraordinary reduction in the death-rate, they have, however, shown such a reduction that would lead one to suppose that some factor was at work to produce such a result.

Statistics and percentage made from Report from Dr. Roger S. Tracy, Register of Records, New York City Board of Health. For January, February, March, April, May, and June.

	CASES REPORTED.	DEATHS RETURNED.	PER CENT.
1886	1763	834	47 $\frac{1}{2}$
1887	2730	1175	43 $\frac{1}{20}$
1888	3965	1188	29 $\frac{9}{10}$
1889	4440	1173	26 $\frac{1}{3}$
1890	2613	710	27 $\frac{1}{3}$
1891	2463	658	26 $\frac{1}{3}$
1892	2854	790	27 $\frac{1}{3}$
1893	2961	924	31 $\frac{1}{3}$
1894	5344	1433	26
1895 (Serum year)	5354	959	17 $\frac{4}{5}$

Statistics and percentage from Mr. S. H. Durgin, Chairman Board of Health, Health Department for Boston. For January, February, March, April, May, and June.

	CASES REPORTED.	DEATHS RETURNED.	PER CENT.
1886	569	154	27 $\frac{1}{15}$
1887	561	154	27 $\frac{1}{2}$
1888	656	228	34 $\frac{2}{3}$
1889	1082	302	27 $\frac{9}{10}$
1890	970	258	25 $\frac{3}{4}$
1891	411	104	25 $\frac{1}{4}$
1892	643	208	32 $\frac{1}{3}$
1893	651	197	30 $\frac{1}{5}$
1894	1001	306	30 $\frac{1}{5}$
1895 (Serum year)	1578	251	15 $\frac{1}{15}$

Comparative statistics of percentage between New York City and Boston, Mass.

	NEW YORK CITY.	BOSTON, MASS.
1886	47 $\frac{1}{2}$	27 $\frac{1}{15}$
1887	43 $\frac{1}{20}$	27 $\frac{1}{2}$
1888	29 $\frac{9}{10}$	34 $\frac{2}{3}$
1889	26 $\frac{1}{3}$	27 $\frac{9}{10}$
1890	27 $\frac{1}{3}$	25 $\frac{3}{4}$
1891	26 $\frac{1}{3}$	25 $\frac{1}{4}$
1892	27 $\frac{1}{3}$	32 $\frac{1}{3}$
1893	31 $\frac{1}{3}$	30 $\frac{1}{5}$
1894	26 $\frac{1}{3}$	30 $\frac{1}{5}$
1895 (Serum year)	17 $\frac{4}{5}$	15 $\frac{1}{15}$

The following was the list of questions sent by me to different physicians who had used the antitoxin :

1. Number of cases?
2. Age?
3. Sex?
4. Result?
5. Was a bacteriologic examination made?
6. The day of disease when injection was made? And quantity?
7. If the case had a fatal termination? How long after injection?
8. Cause of death?
9. Variety of diphtheria :
 Laryngeal { Intubate?
 Tracheotomized? } Before or after injection?
10. If death intubate?
 Tracheotomized?
11. Fauces and larynx?
12. Fauces, nasal, and laryngeal?
13. Nasal?
14. Palatal and faucial?
15. Buccal and faucial?
16. How long after injection did membrane disappear?
17. How long after injection was throat free of membrane?
18. How long after injection was throat free of bacteria?
19. When did you notice a decline in pulse, respiration, and temperature?
20. Did you notice any skin eruption?
21. Did you notice any joint pains?
22. Did you notice any adenitis?
23. Did you notice any otorrhœa?
24. Did you notice any renal complications?
 Albuminuria? }
 Anuria? } Before or after injection?
 Nephritis? }
25. Did you notice any pneumonia?
26. Did you notice any sequelæ? Paralysis, etc.?
27. Did the diphtheria come after scarlatina or measles?
28. Did you practice immunization?
 Adults?
 Children?
29. How much serum at an injection?
 Adults?
 Children?
30. Was bacteriologic examination made of those immunized?
31. Was anyone attacked with diphtheria after immunization? How long after injection?

The questions I most desired answered were those upon which the antagonists of the serum-therapy laid most stress. They were: Skin

eruption, joint pains and swelling, renal complications, sequelæ, and whether immunization protects. The question of diphtheria coming as a complication or an addition, or following scarlatina or measles, was particularly interesting to me, as in my opinion these cases are the most serious, if not the most fatal. As for myself, diphtheria of the larynx (membranous croup) following measles was always in my experience fatal, whether intubated or not, under other methods of treatment. These cases, like the statistics, speak for themselves. I simply copied the reports made to me, curtailing them as much as possible so as to prevent this paper reaching too great a length.

Report from Dr. W. E. Johnson, Waverly, N. Y. Number of cases, 4; 3 females, 1 male. Ages were six, eight, ten, fifty-six years. Result, recovery. No bacteriologic examinations were made; 1 case fauces and larynx; 1 case fauces, nasal and larynx; 2 cases palatal and faucial.

Intubation or tracheotomy unnecessary. The quantity of antitoxin used was 60 c.cm. (6000 immunity units) to case fifty-six years old, with disappearance of membrane on fifth day; 20 c.cm. (2000 immunity units) in each of the other cases, with disappearance of membranes on third day. One case (fifty-six years) showed joint pains, and was followed by paralysis; one case showed albumin after injection. McFarland's (H. K. Mulford Co.) antitoxin used.

Report of Dr. C. P. Adams, Trenton, N. J. Number of cases, 2; females. Ages five, thirty years. Result, recovery. No bacteriologic examination. One death in the family (female, aged three years) one day previous to the doctor's care of these cases; 1 case fauces and larynx, aged five years; 1 case palatal and faucial, aged thirty years.

The quantity of antitoxin used was 20 c.cm. (2000 immunity units) in each case. Membranes disappeared on third day. Pulse and fever declined in twenty-four to thirty-six hours. Adenitis in both cases. Antitoxin used, Behring's and Gibier's. Injections made on the second day.

Report of Dr. I. R. Schoonmaker, Sayre, Pa. Number of cases, 2; 1 male, 1 female. Ages ten, fifty years. Result, recovery; 1 case faucial, buccal, and palatal, ten years; 1 case faucial and laryngeal, fifty years.

No bacteriologic examination. Injection, in adult, on second day, 20 c.cm. (2000) twice injected (4000 immunity units); two injections 10 c.cm. each (2000 immunity units), in child. A death previously

(aged thirty-one years), two days before doctor treated the above cases. The membranes disappeared in child on third day; in adult on the fifth day. Pulse and temperature declined in twenty-four hours. Eruption in child erythematous in character. No sequelæ or complications in either case. Mulford's antitoxin used.

Report of Dr. J. N. Richards, Fallsington, Pa. Number of cases, 1; female, aged three years. Result, recovery.

No bacteriologic examination. Injections were made on the third and fifth days, 10 c.cm. each (2000 immunity units). The membranes began to disappear in from twenty-four to forty-eight hours, and were gone on the third day. The pulse, respiration, and temperature declined in six hours after the second injection. No complications or sequelæ. McFarland's (Mulford's) antitoxin used. The case was one of palatal and faucial variety.

Report of Dr. W. S. Long, Haddonfield, N. J. Number of cases, 3; females. Ages six weeks three days, three and a half years, thirty years. Result, recovery. No bacteriologic examination; 1 case fauces and larynx; 1 case faucial, nasal, and laryngeal; 1 case palatal and faucial.

Injections were made in one case on the third day, another on the fourth day, and another on the second day of the disease. The membranes disappeared on fourteenth day in first, seventh day in second, and in two days in third. Urticaria was noticed in first case. Some paralysis was noted in first two cases. Immunization was practised on third case; 5 c.cm. (500 immunity units) injected; third week after, visual traces of the disease were manifested; 15 c.cm. (1500 immunity units) was then administered. The other received first 10 c.cm. (1000 immunity units), then 15 c.cm. (1500 immunity units).

Report of Dr. A. F. Hyde, Shelby, O. Number of cases, 7; 5 males, 2 females. Result, recovery in 6; 1 death. Bacteriologic examination made in one case.

No.	Age.	Variety.	Quantity and day of injection.	
1	4½ years	larynx and faucial	5 c.cm. (750 units)	3d day Behring's No. 3.
2	33 years	larynx, palatal, and faucial	5 c.cm. "	5th " "
3	14 years	larynx and faucial	8 c.cm. (1200 units)	8th " "
4	13 years	larynx and faucial	5 c.cm. (500 units)	5th " McFarland's.
5	5 years	faucial	5 c.cm. (500 units)	6th " "
6	1 year	faucial	2 c.cm. (300 units)	1st " "
7	3 years	faucial and laryngeal	3 c.cm. (450 units)	2d " Behring's No. 3.

The membranes three days after injection were entirely gone, and began to disappear in twenty-four to forty-eight hours. All these cases suffered from adenitis. In 1 case (No. 2) pneumonia was a com-

plication. As a sequela, 3 cases suffered from paralysis (2 aphonia). Immunization was practised once, 2 c.cm. (300 units), Behring's No. 3 being used, and was successful. The fatal case (No. 5) was septic and moribund, dying seven hours after injection.¹

Report of Dr. S. I. Bassford, Biddeford, Me. Number of cases, 3; 1 male, 2 females. Result, 1 recovery, 2 deaths. No bacteriologic examination made; 1, aged fourteen months, fauces, nasal and larynx; Gibier's; second day, death; 2, aged eight years, fauces and larynx; Behring's; second day, death; 3, aged five years, fauces, nasal, and larynx; Behring's; sixth day, death. Case No. 1 died of pneumonia (catarrhal) twenty-seven days after injection. Case No. 3 died in twenty-four hours, of sepsis. Case No. 1 came as a sequel to scarlet fever. Membranes disappeared in successful case in forty-eight hours.

Report of Dr. Wm. McD. Struble, Trenton, N. J. Number of cases, 11; 8 males, 3 females. One death.

No.	Age.	Variety.	Quantity and day of injection.		
1	15 months	faucial	5 c.cm. 1st, 5 c.cm. 2d (1000 units)	Behring's No. 2.	
2	11 months	faucial	10 c.cm. (1000 units)	1st day	"
3	11 years	faucial and nasal	10 c.cm. "	1st "	"
4	4 years	faucial	10 c.cm. "	1st "	"
5	23 months	faucial and larynx	10 c.cm. "	5th "	"
6	4½ years	faucial	10 c.cm. "	1st "	"
7	5 years	faucial and nasal	10 c.cm. "	1st "	"
8	3 years	faucial and nasal	10 c.cm. "	2d "	"
9	2 years	faucial	10 c.cm. "	1st "	"
10	12 years	faucial	10 c.cm. "	1st "	"
11	2 years	faucial	10 c.cm. "	2d "	"

Case No. 5 died from asphyxia. No bacteriologic examination was made. The membranes disappeared in 6 on third day, in 2 on fourth day, in 2 on fifth day, in 1 on sixth day after injection. Decline in pulse and temperature was noticed in six hours in 2 cases, eight hours in 3 cases, twelve hours in 2 cases, twenty-four hours in 2 cases, and forty-eight hours in 1 case. A slight erythema was noticed in half the cases. All had enlarged glands, but no suppuration. In 2 cases albumin was found. In Case No. 1 (first case treated) temperature fell in six hours, but again rose and continued until throat was free of membrane. As an addition, Dr. Struble sent me an explanation of the method used by him to clinically establish the value of antitoxin. He first used antitoxin on 5 cases with one death (Case No. 5), which could not have recovered under any method of treatment. He then

¹ Three of these cases were reported in the Columbus Medical Journal, April 30, 1895, No. 9, vol. xiv.

treated a second series of 5 cases (these cases coming to him in regular order); of these, 2 died. They were treated without antitoxin, and were of the same character as the first series. He then treated a third series of 5 cases with antitoxin, and all recovered. Two cases of a fourth series, starting the same plan of experimentation, were so serious and so prolonged that he rejected the old plan of treatment and used the antitoxin treatment, although these two recovered.

Report of Dr. G. Metzler, Philadelphia, Pa. Number of cases, 1. Other cases seen and treated by Dr. Metzler appear in report of my cases. Female, aged six years. Recovery. No bacteriologic examination made. Case was one of faucial diphtheria. Injected, on the third day, with 5 c.cm. (500 immunity units) Mulford's antitoxin. The temperature and pulse began to decline within twenty-four hours. The membranes softened within twenty-four hours, and disappeared in three days. Dr. Metzler practised immunization in 11 cases, using 1.5 c.cm. (150 immunity units) in each case. No diphtheria appeared in any.

Report of Drs. Eugene F. and Louis Hauck, St. Louis, Mo. Number of cases, 18; 9 males, 9 females; 2 deaths. Bacteriologic examination made in each case. Ages were from sixteen months to forty-four years. Injections were made, 6 on second, 6 on third, 4 on fourth, and 2 on sixth day of disease; 5 cases fauces and larynx, 1 death; 1 case fauces, nasal, and larynx, 1 death; 12 cases palatal and faucial. Of the 6 laryngeal cases 5 were intubated, with 2 deaths after intubation. The membranes disappeared, 6 in two days, 6 in four days, and 4 in five days. The throat was free from bacteria only after three weeks. Temperature and pulse declined after twelve hours in the majority of cases, some as early as three hours. Joint pains were noticed once. Paralysis came as a sequel three times. Diphtheria came as a sequel to scarlatina once, with recovery. Immunization was practised on two adults and two children. No diphtheria followed in those immunized. Bacteriologic examination was not made on those immunized. Behring's, Gibier's, and Mulford's antitoxins were used.

Report of Dr. S. J. Ottinger, Philadelphia, Pa. Number of cases, 1; male, aged four years and ten months. Result, death. Bacteriologic examination was made. The case was one of laryngeal, faucial, and nasal variety, and was septic. Injected, on seventh day, with 10 c.cm. (1000 immunity units) McFarland's antitoxin. Repeated in six hours with 10 c.cm. (1000 units) more. The child died fifteen hours

after first injection. There was a decline in pulse, respiration, and temperature four hours after second injection. The cause of death, paralysis of the heart.

Report of Dr. G. E. Roos, Scranton, Pa. Number of cases, 25; both male and female. One death. Ages were between six months and ten years. No bacteriologic examination was made. The injections were all made between the first and fourth days, and from 1000 to 2000 units used. In the case that died, death came two days after injection from suffocation from membrane below the tube, a case which the doctor writes should have been tracheotomized; 14 cases palatal and faucial; 9 cases faucial and larynx; 2 cases nasal and faucial.

Of the laryngeal cases 5 were intubated, with one death. The membranes began to disappear in twenty-four to forty-eight hours, and the throat was free in two to eight days. Pulse, temperature, and respiration declined twenty-four hours after injection. One case had pneumonia before injection.

Report of Dr. Alexander Klein, Philadelphia, Pa. Number of cases, 2; females. Ages two and seven years. Result, recovery. Both were palatal and faucial and were injected, on the second day for the seven-year child and on the fourth day for the two-year child, with 10 c.cm. (1000 units) Behring's No. 2. The seven-year child's throat cleared on fourth day; the two-year child's on the third day. Bacteriologic examination was made of both cases, and the throat was pronounced clear of bacteria (KL) in one month for the seven-year and five weeks for the two-year child. Temperature and pulse declined in twenty-four hours; 1 case showed an eruption, and 1 case showed joint pains. Immunization was practised in 11 cases; 4 adults, 7 children. The adults received 300 units, the children received 200 units, and remained well.

Report of Dr. Samuel P. Gerhard, Philadelphia, Pa. Number of cases, 5; 4 females, 1 male. Ages three, four, four, five, and six years. Result, recovery.

Bacteriologic examinations were made at the Laboratory of the Philadelphia Board of Health, and were pronounced true diphtheria. Injections, 7 c.cm. (1400 units), were made twice on third day; once, 10 c.cm. (1000 units), on first day; once, 10 c.cm. (1000 units), on second day; once, 10 c.cm. (1000 units), on fifth day of the disease; 2 cases were fauces and larynx; 1 case was faucial, nasal, and laryngeal; 2 cases were palatal and faucial. The membranes began to disappear in 1 case in forty-eight hours, in 3 cases in three days, and

in 1 case in four days. The throat was free from membranes on the fifth day in all cases, and was free of (KL) bacilli in eight days in 3, and in ten days in 2 cases. The temperature and pulse began to decline in six hours after injection. Skin eruption was noted in 1 case after injection; in a second case before the injection. Adenitis was noted in 3 cases before the injection; in 1 case anuria with oedema after injection. Doctor, however, thinks that the cause of this was exposure to cold and damp; the child was permitted to play in water on a cold day. Two cases had paralysis as a sequel. Immunization was practised in one case, on which a bacteriologic examination was made, no bacilli being found. Mulford's antitoxin was used.

Report of Dr. H. H. Freund, Philadelphia, Pa. Number of cases, 4; 3 males, 1 female. 1 death.

No.	Age.	Variety.	Quantity and day of injection.
1	18 mo.	faucial nasal and laryngeal,	10 c.cm. Behring's No. 2 (1000) 3d day.
2	1 yr.	laryngeal,	10 c.cm. Behring's No. 1 (600) 1st "
3	2 yrs.	faucial and larynx,	10 c.cm. Behring's No. 2 (1000) 3d "
4	4 "	faucial and laryngeal,	10 c.cm. Behring's No. 2 (1000) 4th "

Of these cases 2 were intubated, with 1 death, forty-eight hours after injection. The cause of death being given as oedema of the lungs. In the favorable cases the membranes began disappearing on the third day, and were gone on the fifth day. A decline in pulse, temperature, and respiration was noted in forty-eight hours. One case, which ended favorably, had pneumonia. (Cases reported in *The Medical News*.)

Report of Dr. Chas. D. Spivak, Philadelphia, Pa. Number of cases, 4; 2 females, 2 males. Result, recovery.

No.	Age.	Variety.	Quantity and day of injection.
1	1 year 4 months,	palatal and faucial,	3d day of disease 1000 units.
2	2 years,	fauces, nasal and laryngeal,	2d " " " "
3	8 "	faucial and palatal,	4th " " " "
4	30 "	" "	1st " " " "

No bacteriologic examination made. Laryngeal case intubated several hours before injection. The membrane began to disappear on the second day in Cases 1, 3, 4. In Case No. 2 five days elapsed before membranes disappeared from the fauces, and sixteen days before the tube could be withdrawn and left out. The temperature, pulse, and respiration declined in six to eight hours. Case No. 1 had adenitis. This case came as a sequel to measles.

Report of Dr. J. J. Owen, Philadelphia, Pa. Number of cases, 2; 1 male, 1 female; ages two years. 1 death. Case No. 1,

laryngeal, 10 c.cm. Behring's No. 2. Intubated. Death in forty-eight hours. Case No. 2, palatal and faucial, 17 c.cm. (1700 units) Behring's No. 2. Injected on fourth day.

The case that recovered required two injections. Temperature and pulse declined four hours after each injection from 103° to 99°. The laryngeal case was injected on the first day.

Report of Dr. George A. Muehleck, Philadelphia, Pa. Number of cases, 26. 3 deaths.

I am somewhat familiar with Dr. Muehleck's work, he being the first to have used antitoxin in Philadelphia, Pa. Dr. Muehleck makes his own bacteriologic examinations in most all the cases treated by the antitoxin, and also in those immunized. He has immunized 40 cases, all children, in half of which the Loeffler bacillus was found, and not a single case showed any visual signs of the disease. In his practice he used Gibier's antitoxin in 5 cases, Behring's antitoxin in 4 cases, and Aronson's in 17 cases. The erythematous rash followed in all cases upon which Gibier's antitoxin was used. Of Behring's he used 5 c.cm. of No. 3, equivalent to 750 units. The same amount of Aronson's was used.

No.	Age.	Sex.	Variety.	Injection.	When Injected.
1	4 yrs.	M.	laryngeal,	Aronson's	2d day.
2	3 "	M.	palatal and faucial,	Gibier's	2d "
3	6 mos.	M.	" "	"	2d "
4	2 "	F.	" "	"	2d "
5	5 "	F.	palatal and faucial, nasal and laryngeal,	Aronson's	6th "
6	7 "	M.	palatal and faucial,	Gibier's	1st "
7	4 "	M.	buccal and faucial,	"	1st "
8	9 "	M.	palatal and faucial,	Aronson's	2d "
9	9 "	M.	nasal and faucial,	"	2d "
10	6 "	M.	faucial and palatal,	"	2d "
11	1 " 9 "	F.	fauces and larynx,	Behring's	3d "
12	3 "	M.	faucial and palatal,	"	1st "
13	9 "	M.	" "	Aronson's	2d "
14	5 "	F.	laryngeal,	"	2d "
15	6 "	F.	faucial and palatal,	"	2d "
16	12 "	M.	fauces and larynx,	"	2d "
17	4 "	F.	laryngeal, nasal, and faucial,	Behring's	3d "
18	3 "	M.	laryngeal,	"	3d "
19	7 "	F.	" "	Aronson's	3d "
20	5 "	M.	palatal and faucial,	"	4th "
21	3 "	F.	" "	"	2d "
22	1 " 2 "	M.	" "	"	2d "
23	4 "	M.	" "	"	2d "
24	2 "	F.	laryngeal,	"	6th "
25	2 "	F.	" "	"	2d "
26	2 "	F.	" "	"	2d "

In the cases that died the injections were all made a few hours before death. The membranes began to disappear in the faucial and

palatal cases in twenty-four to thirty-six hours; in the laryngeal, forty-eight to seventy-two hours. The throat cleared about five to six days in the faucial, and from seven to ten days in the laryngeal. The throat cleared of bacteria in four to five weeks.

The temperature, pulse, and respiration declined within four to six hours. Albumin was found in 12 cases, the most severe ones, before injection, which did not appear to have any influence on the symptom. Paralytic (faucial) symptoms came as a sequel in about 12 cases, but disappeared very soon. Three cases were a sequel to measles, 1 of these died. In the cases immunized Dr. Muehleck used Aronson's, Mulford's, and Solis-Cohen's. He gave from 100 to 300 immunity units. In no single case was there any outbreak. (4 cases reported in *The Medical News*. Dr. Muehleck presenting a paper before the College of Physicians.)

Report of Dr. Edwin Rosenthal's Cases. Number of cases, 78. 2 deaths.

The 2 deaths are reported with Drs. Owen's and Freund's cases, and were entered by me in my list because they were intubated by me. Most of my cases had a bacteriologic examination made by Dr. A. Klein, by Dr. B. Meade Bolton, or Gillespie or Pease, in the Bacteriological Laboratory of the Bureau of Health, and by Dr. George A. Muehleck, in his private laboratory. I had also the case immunized examined with the result that over 50 per cent. showed the Klebs-Loeffler bacilli. In several cases, where I had given curative doses of the serum, no specific bacilli were found on bacteriologic examination; the patient showed no bad symptoms on receiving this dose. I have used Aronson's, Roux's, Gibier's, Behring's, Mulford's, and Solis-Cohen's antitoxin. In those immunized not one showed visual traces of the disease, even when constantly brought in contact with those so affected. Mulford's antitoxin showed equal value with Behring's No. 2, with which I was most familiar, and in administration I used the same quantity, c.cm. for c.cm.

The cases treated were 31 males, 47 females, all white. Their ages were: 8 between one and two years old, of which 5 were intubated, with 1 death; 10 between two and three years old, of which 5 were intubated, with 1 death; 5 between three and four years old, of which 1 was intubated; 15 were between four and five years old, of which 2 were intubated; 3 were between five and six years old, of which 1 was intubated; 4 were between six and seven years old, of which one was intubated; 2 were between seven and eight; 3 between

eight and nine; 2 between nine and ten; 2 between ten and eleven; 1 between eleven and twelve; 2 between twelve and thirteen; 1 between thirteen and fourteen; 1 between fourteen and fifteen; 2 between fifteen and sixteen; 1 between seventeen and eighteen; 1 each for twenty-two, twenty-three, twenty-four, twenty-six and twenty-eight years; 5 between thirty and thirty-one; 4 between thirty-two and thirty-three years; and 1 each between thirty-six and and thirty-seven and forty and forty-one years of age.

There were 11 laryngeal, 4 intubated, 1 death; 12 faucial and laryngeal, 8 intubated, 1 death; 3 faucial, nasal, and laryngeal, 3 intubated; 1 faucial and nasal; 3 faucial and palatal; 48 faucial. Of these cases the most received 10 c.cm. (1000 immunity units)—when Behring's or Mulford's antitoxin was used—at a dose; repeated in twelve to twenty-four hours, if necessary; if other antitoxin was used, an equivalent was administered, though some received as low as 600 units as a curative dose. In some cases Aronson's or Mulford's or Solis-Cohen's antitoxin was used as the first dose and Behring's antitoxin as the second dose. I noticed no joint pains, and a skin rash was noted in 10 cases only. Albumin was detected in only 8 cases and had nothing to do with the serum. I invariably examine the urine, as I had been taught since 1885 that albumin was a complication of diphtheria and those cases so affected were serious, if not fatal. I practised immunization on everyone willing to receive it. Dr. J. Solis-Cohen, as well as Mr. Campbell, of the H. K. Mulford Company, kindly furnished the antitoxin for my poor cases. Over 200, probably one-third adults, received an immunizing dose, about 100 to 200 (if the Loeffler bacillus was found) at a dose. In extraordinary cases, like a pregnant woman in the last days of pregnancy, they received 400 to 600 units; of this description, a case was immunized by Dr. A. Klein with success.¹ I also immunized phthisical as well as otherwise affected individuals, and have yet to see one case show visual signs, although one-half the cases by bacteriologic tests showed the bacilli; 1 case had ozæna as a sequel. Aphonia was a sequel in several cases of laryngeal.

Injections were made on the first day of the disease in 18 cases, on the second day in 30 cases, on the third day in 22 cases, on the fourth day in 4 cases, on the fifth day in 1 case, on the sixth day in 2 cases, and on the seventh day in 1 case. In the faucial cases the membranes

began to disappear on the second day, and were entirely gone by the fifth day. In the laryngeal cases stenosis was relieved on the third day; in those cases intubated the tube was allowed to remain until the fourth day; 1 case necessitated its use for sixteen days. Bacteriologic examinations showed the bacilli one month after injection. Anæmia or other sequelæ were never noticed; in the laryngeal cases the same pallor and emaciation were seen, but in two or three days were entirely gone.

Report of Dr. L. Wolff, Philadelphia, Pa. Number of cases, 5; 3 females, 2 males. Ages, two to six years. Result, recovery.

Bacteriologic examinations were made in every case in the Laboratory of the German Hospital. Injections were made on the second day in 4 cases, and on third day in 1 case. The quantity used was 10 c.cm. (1000 units) Behring's No. 2. Immunization was practised once on a child, and 2 c.cm. (200 units) were injected, with success; 2 cases were laryngeal and fauces, both intubated, one before and one after injection; 3 cases were palatal and faucial.

The membranes began to disappear in from twenty-four to seventy-two hours, and the throat was clear in three to four days. It was not ascertained how long after the throat was clear of bacilli. No skin eruptions or joint pains were noted, but adenitis was a symptom. Albuminuria was noted twice, before and after injection; 1 case was followed by paralysis (1 case published in *Medical News*).

Report of Dr. John Sebastian Miller, Philadelphia, Pa. Number of cases, 18; males and females equal. Ages, one to ten years. Result, recovery. Used Gibier's, Behring's, and Mulford's.

Immunized 8 cases; no infection, all cases being successful; 7 cases were laryngeal and faucial; 2 were nasal and faucial; 3 were faucial, buccal, and palatal; 6 were faucial.

The membranes began to disappear thirty-six hours after injection, and were entirely gone in three to four days. Bacteriologic examinations were made in 12 cases. The injections were made equally on the first, second, and third days. Stenosis was relieved in the laryngeal cases on the third day; 4 cases had adenitis; albumin was found in but 1 case, and had no significance; as a sequel in 5 laryngeal cases of aphonia lasting one week occurred. As an addition to his report, Dr. Miller observes: "I have not lost a single case since the antitoxin period, and most of my cases were very seriously ill; a death now to me would be an exception. Previously to the antitoxin period I looked upon diphtheria with a great deal of fear, and deaths were a common

occurrence." Despite intubation, tracheotomy, etc., his percentage of deaths was always large. Whilst his cases were always serious, he can find no difference in the gravity of his present cases, except that they recover.

A summary of these reports shows the following: Cases reported, 222, almost equally divided as regard sexes; adults, 44; children, 178. There were 13 deaths, showing a mortality of $5\frac{1}{2}\%$ per cent.

There were faucial, 63, no deaths; laryngeal, 20, 2 deaths; fauces and larynx, 50, 3 deaths; faucial, nasal, and laryngeal, 14, 7 deaths; faucial and nasal, 6, no deaths; buccal, faucial, and palatal, 13, 1 death; faucial and palatal, 56, no deaths. Of the 84 laryngeal cases 12 died; 31 were intubated, with 5 deaths.

The deaths were as follows:

1.	Died	7 hours	after injection	on 7th day.
2.	"	27 days	"	"	(from pneumonia)	.	.	on 2d	"
3.	"	24 hours	"	"	.	.	.	on 7th	"
4.	"	10	"	"	(faucial, nasal, and laryngeal)	.	.	on 5th	"
5.	"	15	"	"	(sepsis)	.	.	on 7th	"
6.	"	7	"	"	"	.	.	on 6th	"
7.	"	4	"	"	"	.	.	on 6th	"
8.	"	5	"	"	"	.	.	on 4th	"
9.	"	24	"	"	(intubated)	.	.	on 4th	"
10.	"	2 days	"	"	"	.	.	on 4th	"
11.	"	18 hours	"	"	" (spread of membrane)	.	.	on 2d	"
12.	"	2 days	"	"	"	.	.	on 2d	"
13.	"	31 hours	"	"	"	.	.	on 2d	"

Those writers antagonistic to the serum treatment have laid particular stress upon the eruption, joint pains, adenitis, otorrhœa, renal complications and sequelæ, as paralysis, etc. The following are the answers to these questions: Skin eruptions, 32 cases; joint pains, 3 cases; adenitis, 14 cases; otorrhœa, no cases. Renal complications: Albumin, 24 cases before, 2 cases after injection; anuria, 1 case after injection; nephritis, no cases. Sequelæ: Paralysis, 16 cases, counting 12 cases of aphonia.

These proportions above given are, sure, not a contraindication for the further use and observation of this treatment.

More stress has been laid upon the question of immunization. In Philadelphia alone, I think, this question can receive the fairest test. The Spartan simplicity of the Board of Health's methods, of our city, should receive the most profound attention of those who have no faith

in immunization. The Philadelphia Board of Health's methods are unique, to say the least, to prevent the spread of contagious diseases. They lock the healthy with the sick, under lock and key, with what is termed strict quarantine, and a policeman at the front and rear of the house. They do not permit the healthy to come forth into the streets to enjoy the air, for they might pollute the atmosphere and spread contagion, but keep them penned in (and especially in our tenement system, you can imagine), so that the unfortunates form a very predisposing incentive for dangerous bacteria. I have here cards from Dr. Bolton (our bacteriologist of the Board of Health) representing two families. There was but one sick in each, and the rest were immunized. Whilst some of those immunized showed the Loeffler bacilli by bacteriological test, no visual traces were ever seen, nor were any symptoms noted in those or the rest that were so treated. The same experiments were made by Dr. Muehleck with the same results.

There were 276 cases immunized. Of these, 64 were adults and 212 children. One case was reported to me as becoming infected three weeks afterward. (Dr. W. S. Long, Haddonfield, N. J.) This case was an adult, aged thirty years, upon whom 5 c.cm. (500 units) were injected. Visual traces of the disease being seen, 15 c.cm. (1500 units) were injected; the case was one of the faucial-palatal variety. Of the 276 cases, 201 showed the bacilli, or other evidence that was suspicious.

In pursuing my work I had no assistance from the different hospitals (the Boston City Hospital, South Department, excepted) to make comparisons. I therefore adopted the classification of Lennox Browne, London, Eng. (*The Journal of Laryngology, Rhinology, and Otology*), as most satisfactory to myself and of some value and interest, as it would place in comparison his report of a hospital—The Metropolitan Fever Hospital—and the report of private practice. Inasmuch as Lennox Browne sees no value in the antitoxin treatment, and may be classed as an antagonist, the reports placed in juxtaposition have an increased interest. I shall, therefore, follow his methods as follows:

Series A refers to cases under former treatment. Series B under serum treatment. Actual mortality is the same in both series. The serum employed is that provided by the British Institute of Preventive Medicine.

1. Mortality of age periods.

Age.	A.			B.			My own statistics.		
	Number of cases.	Deaths.	Per ct.	Number of cases.	Deaths.	Per ct.	Number of cases.	Deaths.	Per ct.
Under 5 years . .	51	42	43.1	43	23	53.48	110	7	6.40
5 to 10 " . .	28	3	10.7	37	3	8.1	68	6	8.74
Over 10 " . .	21	2	9.5	20	1	5.0	44		

2. The day of the disease on which treatment was commenced.

Any treatment when begun early is almost sure to be successful in almost all disease, is an aphorism which will not hold good in diphtheria. Though Lennox Browne, Winters, Rosenbach, and some others of those antagonists to serum-therapy are contrary. As a matter of fact, prognosis in diphtheria is almost an impossibility. We know how in an hour cases can become septic, or how in a moment a sufferer from diphtheria may perish. No matter how bright the outlook may be at the beginning or how mild a case it might be, no one can predict an end. Therefore, any reason given against the assertion of its advocates—"the earlier antitoxin is used the more certain its success"—is fallacious and misleading. "The following figures (A and B) show that there is no warrant for special application of so general a law to the case of the serum remedy, the dates on which serum commenced corresponding so closely." (Lennox Browne.) I think there is warrant for special application.

Day of commencement of treatment.	Series A. Number of cases.	Series B. Number of cases.	My own number of cases.
1	2	2	43
2	29	24	84
3	22	32	61
4	20	17	19
5	8	9	4
Over 5	19	10	11

Browne makes this assertion : In hospitals for diphtheria, where it is the rule for nurses who have the least symptom of sore throat to present themselves to the medical superintendent for immediate examination, and where the disease is, therefore, attacked at once, a fatal result is almost unknown, and this under the former method of treatment. In the hospital where these observations were made, 42 cases of diphtheria have occurred in the staff during the last five years without a fatal result. I wish I could give some statistics of

the hospitals in comparison to this. In my own practice at present I immunize the nurse, and accomplish the same purpose.

3. The following figures show the *prolongation of life in cases with fatal results* :

Day of death.	Number of deaths.		
	Series A.	Series B.	My own statistics.
Within 24 hours.	11	3	7
2d day.	2	1	4
3d "	4	3	1
4th "	3	4	0
5th "	1	2	0
6th "	3	1	0
7th "	1	1	0
8th "	1	4	0
9th "	0	1	0
10th "	1	0	0
16th "	0	1	0
21st "	0	1	0
27th "	0	0	1
32d "	0	1	0
38th "	0	1	0

4. *The site of membrane* is to be considered as an important indication of the series of cases, and although Series A has fewer examples of nasal diphtheria—the most fatal form—*per contra*, it has many more examples in which membrane extended to the larynx and a larger number of tracheotomies. (Lennox Browne.) I might say the same of my series, with the difference of intubation for tracheotomy, where intubation or tracheotomy was not necessary, all laryngeal cases recovered; so much for statistics :

Site of membrane.	Series A.	Series B.	My own.
Fauces	60	65	63
Larynx	2	0	20
Fauces and larynx	16	3	50
Faucial and nasal	17	28	6
Faucial, nasal, and laryngeal	1	2	14
Nasal	1	1	0
Hard palate	0	1	0
Faucial and palatal	1	0	56
Faucial and buccal	1	0	13
Faucial and vulval	1	0	0

Browne adds : " With regard to *nasal* diphtheria, whether in association with the fauces or larynx, or both, we have found in 1000 cases, tabulated with regard to site and other items of interest, that

this variety was fatal in 67 per cent., and in the present comparison we find in Series B a total of 31 cases of this class, 16 of which ended fatally—in other words, 50.16 per cent. This in favor of serum, for under the older method of treatment, as represented in Series A, out of a total of 19 cases 12 died, or 63.15 per cent.” My own statistics show but 20 cases, of which 7 died—a mortality of 35 per cent. Our conditions may, however, have been different, still it shows by Browne’s own figures the value of serum-therapy.

“In the cases in which the larynx was involved, in Series A., 7 died without operation out of a total of 18; these included 1 case which died within twenty-hours of entrance to the hospital, intubation having been performed previous to admission; 4 tracheotomies were performed, of which number 2 died.

“In Series B there were 5 cases of laryngeal diphtheria, and of these 2 died; in 1 of the fatal cases tracheotomy was performed. These numbers are certainly too small to deal with, but evidence from other sources is distinctly in favor of serum treatment with regard to laryngeal diphtheria.” (Lennox Browne.)

In my statistics there were 84 cases, of which 12 died; 14.34 per cent.; 31 were intubated, of which 5 died; 16.23 per cent. I think in laryngeal diphtheria the specific action of antitoxin can be proven. In a former paper at Chambersburg, Pa., before the State Medical Society (*Medical News*, June 8, 1895), I pointed out this fact; further experience has more firmly impressed this upon me. Besides, in those cases intubated antitoxin exerts such a specific action that the length of time a tube should remain in the larynx can be known to a certainty, where formerly we never could tell when the tube should be removed. We permitted it to remain (except where it was removed by coughing) at least one week before we thought of removing it. Now, on the fourth day all tubes are removed, and in the majority of cases reinsertion is unnecessary. The same was noticed by Bökei, whose cases I also quote.

5. *The day of treatment on which the membrane commenced to separate:*

Day.	Series A (50 cases).	Series B (100 cases).	My own (222 cases).
1	10 or 20 per cent.	1 per cent.	25 or 11.25 per cent.
2	13 or 26 “	28 “	51 or 23 “
3	18 or 36 “	36 “	72 or 33 “
4	7 or 14 “	14 “	73 or 33 “
5	2 or 4 “	2 “	1
7	0	1 “	0
12	0	1 “	0

6. *The day on which the throat was declared free of membrane:*

Day.	Series A.	Series B.	My own.
2	4	1	17
3	13	4	71
4	14	9	73
5	14	18	39
6	8	18	7
7	6	10	5
8	5	2	5
9	1	1	1
10	1	1	0
11	1	0	1
12	0	2	0
13	0	2	0
14	0	2	1
16	0	2	2
17	0	1	0
24	0	1	0
28	0	1	0
29	0	1	0

7. *Skin eruptions and joint pains.* These symptoms were known to Behring, who (*Das neue Diphtheriemittel*, Behring, Berlin, O. Häring, 1894) says it might be due to the serum, but not to the antitoxin. He would investigate this matter and see what the reasons were. Probably the serum may have been used too soon before the ac. carbol. had settled. At any rate, I cannot see anything dangerous in these symptoms, as they pass so rapidly away without treatment. Browne saw eruptions frequently, and in his series of cases saw 4 cases of joint pains. In my series eruptions were noted 32 times, joint pains 3 times.

8. *Adenitis* was observed in 18 cases in Series A and in 28 cases in Series B. In my cases it was noticed 14 times. In Browne's statistics the proportion of cases which went on to suppuration was about equal in the two. As far as I have learned no case suppurated. In connection with this question of suppuration, Browne mentions that there were 2 cases of abscess at the site of injection. We have never noticed any.

9. *Otorrhœa* was never noted, but *ozœna* was in our cases.

10. *Renal complications.*

a. *Albuminuria* was found by Browne 38 times in Series A and 50 times in Series B. It was noted in my cases 26 times. This, however, may be incorrect, as many of the cases were not examined.

b. Anuria was noted once. It was noted twice in Series A and 7 times in Series B.

c. Nephritis was not noted in this group of cases. In Series B of the 7 cases that perished from anuria, 5 were proved to have nephritis by post-mortem examination.

11. *Heart failure* was not so specially noted in this group. Browne notes 4 cases in his Series B. Of other causes of death in Series B, 6 were due to broncho-pneumonia, and 1 to septic peritonitis. Broncho-pneumonia was the cause of 1 death in my group. Sepsis the cause of several.

12. *Paralytic sequelæ*. 14 per cent. of cases in all cases, including Series A and B, is noted by Browne. In our group it has occurred 16 times. Baginsky remarked at Munich that "paralysis is more frequent under antitoxin than before." Lennox Browne does not think so by his series, nor is such the fact by mine.

It is to be regretted that the experience of Lennox Browne was such as to impress him unfavorably. His paper, from which I quote so largely and the style which I follow so closely, impressed me as no other monograph on this subject has. The methods of hospital treatment may in some way act contrary to our expectations, and on the whole be very disappointing. The only other hospital that I care to quote—for it is the only one that I received an affirmative answer from—is the Boston City Hospital, South Department. I received from Dr. Calvin Gates Page, the interne, a short *résumé*: "They used since July 1st antitoxin produced by the Boston Board of Health on 113 cases. There have been 90 recoveries and 23 deaths. Of the 23 deaths, 15 were hopeless cases when admitted. Of the 98 cases that received seasonable treatment but 8 died, showing a mortality of less than 8 per cent., whereas formerly the mortality from diphtheria has been 50 per cent."

In the *Deutsche medicinische Wochenschrift*, April 11, 1895, is a report from Dr. Johann Bökei ("Meine Erfolge mit Behring's Diphtherie-heilserum," read before the Budapest Königl. Aerztevereins, February 9, 1895) of the Budapest Stephanie Kinder Hospital (Diphtheria Department). This report is most interesting, as Dr. Bökei studied his cases as I mine. Seeking those symptoms upon which the antagonists of antitoxin lay such particular stress, the following is a brief summary:

Number of cases, 120; deaths, 31; 25.5 per cent. In cases not operated the mortality was 14 per cent. In those operated (intuba-

tion) the mortality was 43 per cent. The ages were: Under one year, 1 case; over one year, 22 cases; over two years, 22; over three years, 24; over four years, 18; over five years, 13; over six years, 6; over seven years, 7; over eight years, 2; over nine years, 1; over ten years, 1; over eleven years, 2; over twelve years, 1.

The variety of diphtheria was as follows:

Variety.	Cases.
Faucial.	41
Faucial and nasal.	13
Faucial and conjunctiva	1
Faucial and vulvitis	2
Laryngeal (not operated)	14
Laryngeal (operated)	49

His 31 deaths were in children of the following ages: Under one year, 1 case; over one year, 10; over two years, 7; over three years, 4; over four years, 3; over five years, 1; over six years, 1; over seven years, 3; over ten years, 1 case.

Of these deaths, 18 (therefore over one-half) were in the first two years.

Death occurred as follows: 1 case five hours after admission, 1 case twelve hours, 1 case eighteen hours, 2 cases twenty hours, 1 case twenty-three hours, 5 cases twenty-four hours, 1 case forty hours.

The cause of death was: Sepsis in 5 cases, descending croup in 13, pneumonia in 7, paralysis of the heart in 3, nephritis in 1, scarlatina in 1, tuberculosis in 1.

In all his cases Bökai saw not one sequel (paralysis of the heart, post-diphtheria, paralysis nephritis), but all cases when cured recovered fully.

Bökai studied particularly albuminuria, and found it in 37 cases; the duration was: In 6 cases one day, in 5 cases two days, in 5 cases three days, in 6 cases four days, in 3 cases five days, in 4 cases six days, in 3 cases seven days, in 1 case eight days, in 1 case eleven days, 1 case twelve days, 1 case thirteen days, 1 case twenty-two days.

The skin rash was noticed in 11 cases: 1 in three days after injection, 3 in six days, 1 in eight days, 3 in ten days, 1 in eleven days, 1 in twelve days, 1 in thirteen days.

The duration of the erythema was: In 4 cases one day, in 2 cases two days, in 1 case three days, in 2 cases five days, in 1 case seven days, in 1 case eight days.

In the 11 cases the erythema disappeared 6 times, without any symptom, 5 times with fever, and 4 cases the fever was very high.

Bökai immunized 70 cases with success, and describes an epidemic in another department of the hospital (measles) where diphtheria infected those so affected; 14 remaining cases were immunized without one outbreak of diphtheria.

Other statistics are familiar to you all. The journals are full of them. In the *Therapeutische Monatshefte*, July, 1895, page 372, most of the late cases are described of those occurring in Europe. G. C. Crandall, St. Louis, Mo. (*Journal American Medical Association*, July 27, 1895), gathered the statistics to that date, including Heidelberg, Prague, Vienna, Berlin, Munich, Leipsic, Halle, Paris, London, New York, and Boston. The whole number of cases were 4022; mortality, 17.1; previous mortality, 42.0.

As those whose records have placed themselves as opposed to the serum-therapy speak of these statistics as misleading (Dr. C. L. Schleich and Dr. A. Gottstein, "Immunität, Infections Theorie and Diphtherie Serum," Berlin, 1894) and false; that many cases are reported now that would have never been reported, and were of mild character, hence the increase of cures, I have investigated this subject further and found that whilst, in truth, there may be some foundation for this assertion, other cases not reported, and the most serious (membranous croup) would equalize this. Schleich gives the reason: a fear of quarantine and its necessary evils as the cause. Dr. Welsh, Philadelphia, told me different: his theory was to swell the statistics. However, as it is now conceded that membranous croup is diphtheria, and should so be reported, I asked Dr. Roger S. Tracy, Register of Records, New York City, for a report of deaths from croup for New York, and Dr. S. H. Durgin, Chairman, Board of Health of Boston, for the deaths from croup for Boston. These returns I have added to the former returns received, and I therefore give what I think should have been the true statistics.

Deaths from croup for January, February, March, April, May, and June:

	New York.	Boston.
1886	478	37
1887	563	55
1888	401	73
1889	369	66
1890	304	43
1891	307	23
1892	361	31
1893	357	39
1894	338	28
1895	187	36

REPORT OF DEATHS FROM CROUP. NEW YORK BOARD OF HEALTH.
Through ROGER S. TRACY, M.D., Register of Records.

Month.	1886	1887	1888	1889	1890	1891	1892	1893	1894	1895
January	97	115	92	69	46	66	61	90	64	40
February	87	93	77	67	59	49	68	63	50	33
March	102	105	76	69	56	67	62	66	62	36
April	72	98	51	61	65	50	76	49	61	32
May	56	95	57	61	44	44	63	56	65	28
June	64	57	48	42	34	31	31	33	36	18
July	60	27	28	35	28	37	52	30	22	28
August	49	22	29	25	26	22	30	41	20	29
September	48	47	37	38	24	48	42	28	21	
October	89	67	32	43	32	66	68	50	29	
November	126	82	43	55	53	59	57	37	41	
December	118	81	69	40	54	70	60	45	40	

REPORT OF DEATHS FROM CROUP. BOSTON HEALTH DEPARTMENT.
Through S. H. DURGIN, M.D., Chairman Board of Health.

Month.	1886	1887	1888	1889	1890	1891	1892	1893	1894	1895
January	7	20	18	12	13	6	7	9	8	10
February	4	12	14	12	5	3	6	9	5	10
March	13	6	14	14	8	5	5	9	4	5
April	1	7	8	13	6	2	5	4	6	4
May	5	8	11	9	5	6	5	5	1	3
June	7	2	8	6	6	1	3	3	4	4
July	7	2	2	4	1	1	2	2	4	1
August	5	3	8	2	1	2	1	6	5	
September	6	3	3	11	4	1	3	1	1	
October	10	9	5	11	2	6	4	5	7	
November	14	10	13	8	5	7	12	4	6	
December	15	12	15	17	5	13	12	13	10	

Since 1890 diphtheria and membranous croup have been considered one in Boston; and in New York I think 1892 was the year when croup was declared contagious. The altered percentages are as follows:

	New York.		Boston.	
	Without croup.	With croup.	Without croup.	With croup.
1886	47 $\frac{1}{3}$	58.9	27 $\frac{1}{15}$	31.5
1887	43 $\frac{1}{20}$	52.9	27 $\frac{1}{2}$	32.4
1888	29 $\frac{9}{10}$	36.5	34 $\frac{3}{4}$	41.3
1889	26 $\frac{1}{3}$	32 $\frac{1}{12}$	27 $\frac{9}{10}$	32.1
1890	27 $\frac{1}{6}$	34.8	25 $\frac{3}{4}$	

Croup and diphtheria.		
Reported together under diphtheria.		
1891	26 $\frac{1}{3}$	25 $\frac{1}{4}$
1892	27 $\frac{1}{3}$	32 $\frac{1}{4}$
1893	31 $\frac{1}{4}$	30 $\frac{1}{2}$
1894	26 $\frac{4}{5}$	30 $\frac{1}{5}$
1895	17 $\frac{4}{5}$	15 $\frac{1}{5}$

These statistics and cases explain themselves. What conclusions are drawn therefrom can easily be given. Clinical evidence is in

favor of antitoxin, notwithstanding the contrary opinions expressed. For the different monographs upon this subject I am very much indebted to my cousin, Dr. A. Baer, of Berlin, who has also furnished me with my Behring's antitoxin. I am also under obligations to Dr. Roger S. Tracy, of the New York Board of Health, and Dr. S. H. Durgin, of the Boston Board of Health, for their kindness in furnishing me with statistics, also to Dr. Page, of the Boston City Hospital, South Department, for his statistics.

I am in favor of the antitoxin treatment of diphtheria. As an evidence of the correctness of my position I have given the reports of numerous physicians, the reports of three different hospitals, the extended reports of the cities of Boston and New York, and the combined statistics of Heidelberg, Prague, Vienna, Berlin, Munich, Leipzig, Halle, Paris, London, New York, and Boston. Philadelphia has no statistics to present.

DISCUSSION.

The PRESIDENT invited Dr. B. Meade Bolton, Director of the City Bacteriological Laboratory, to open the discussion.

DR. BOLTON said: I would like, in the first place, to make a personal explanation. Dr. Rosenthal seems to be under the misapprehension that it is within my power to regulate quarantine of infected localities in the city, whereas this is entirely out of my power. If it ever should be in my power to do so, I should endeavor to correct the faults Dr. Rosenthal complains of. My only power is to examine cultures and to make reports upon the same. All other regulations in this direction were made before I came into office, and have been continued since that time without any alteration, so I am without responsibility for them.

The statistics offered by Dr. Rosenthal seem to be very convincing in spite of the difficulties surrounding this method of deciding questions of treatment. Many which have been published are of little value, but the most satisfactory I have yet seen in print appeared in the *Deutsche medizinische Wochenschrift*, 1895, No. 32, where there is a report of a study of ten thousand cases of diphtheria and a comparison drawn between those treated by antitoxin and those not so treated, with a total mortality of about 11 per cent. About 6000 cases treated with antitoxin gave a mortality of 9½ per cent.; about 4000 cases not so treated gave a mortality of 14½ per cent. These are the best that have yet been gathered. The weight of authority seems to be increasing in favor of this method of treatment in uncomplicated diphtheria. Escherich has lately come out in favor of the antitoxin, and his name will bring a good deal of weight, as he is a very careful observer. With regard to the complicated cases, it is evident that less favorable results must

follow the treatment than with the uncomplicated ones. It is hardly fair to demand that the diphtheria antitoxin should cure these complicated cases any more than it would to expect quinine to cure a patient when in addition to malaria he has phthisis. The quinine will cure malarial affections, but not other infections which may accompany them, and diphtheria antitoxin, in the same way, will only be successful in uncomplicated diphtheria.

I might refer to one point that Dr. Rosenthal mentioned. It is that there is no connection between the treatment of diphtheria by its antitoxin and the inoculation of animals with toxins. I recall the fact that Dr. Theobald Smith, of Washington, D. C., was the first to isolate the bacillary products from living fluids for therapeutic purposes; others had made extracts but Dr. Smith was the first to use the living fluids.

Dr. Rosenthal stated that Buchner claims that the toxic substance resides in the body of the micro-organism. This is undoubtedly true in the comma bacillus of cholera. But it is not true of others, notably of the tetanus bacillus. In tetanus if liquid cultures are filtered through porcelain filters the filtrate alone produces the disease; the bacilli left on the filter are harmless on inoculation. With other diseases the results are various, for in some the toxin resides in the bodies and in others in the fluids.

The laboratory evidences in regard to this matter of immunity are very convincing; it is only necessary to observe the effect of the injections to be satisfied of their protective influence.

Dr. Rosenthal also mentioned that the antitoxins were entirely specific in their action. This is not exactly correct. Roux has found lately that the antitoxin of tetanus is also of value in cases of poisoning by venomous serpents, and it has been found serviceable in other kinds of poisoning, so that in a limited sense, antitoxin is not specific. I might also mention the use of erysipelas and prodigious toxins in the treatment of cancer, and other illustrations of similar character.

With regard to the theory on which this immunity is based, there are some very interesting theories suggested. The first one, which was pretty generally accepted at first, was Pasteur's exhaustive theory. The idea was that in every animal there was a peculiar pabulum, which was exhausted by an attack of the infectious disease, so that the organism became unsuitable for subsequent growth of the infectious agent. In the retention theory of Chauveau, Wernicke and others it is assumed that the products of the growth of the bacteria are retained and make the tissues unsuited to the growth of bacteria. Grawitz's idea is that there is a fight between the bacteria and the cells, and that the cells of the body gained strength after an attack of the disease so as to successfully resist another invasion. This explanation is not sufficient in one direction and explains too much in another; it fails to explain cases of relapse, on the one hand, and also why the cells thus strengthened were not able also to resist attacks of other diseases, on the other. Then there is Buchner's theory. He attributes immunity to a reaction on the part of the body against the poison of the micro-organisms. Wolffberg expresses the idea more precisely. He holds that one set of cells is destroyed in the conflict and thrown off, as is the case with smallpox, where the susceptible cells are destroyed, leaving the insusceptible

cells to propagate. This idea is analogous, on a small scale, to an epidemic in a city where the susceptible persons are destroyed or become immunized, and the community is consequently free for a time from subsequent invasion.

Brieger, Kitasato, and Wassermann are of the opinion that in every culture of bacteria there are two substances, viz.: a toxic substance and an antitoxic substance. In recovery from disease the toxic substance is destroyed by certain glands of the body, notably those rich in cells, like the thymus, and the antitoxin remains. There are certain facts which speak in favor of this view. Cultivating certain bacteria in extracts of thymus gland produces a substance which can be used to immunize animals. The addition of trichloride of iodine to cultures has the same effect, also the passage of electricity through cultures.

Behring's hypothesis is that the antitoxin is produced by the cells of the body under the stimulus of the toxin, and Metschnikoff holds that these cells are the phagocytes or white blood-corpuscles. Behring is inclined to accept Metschnikoff's view.

DR. EDWIN E. GRAHAM: With regard to the question whether the diphtheria antitoxin reduces the mortality from diphtheria, I think that those who have followed the subject carefully can arrive at only one conclusion—that the mortality is reduced. As regards statistics, they should be made up in a certain way in order to be worth anything at all. For instance, if we take the returns of the Health Office of the city of Philadelphia of different years, such as 1891, 1892 to 1895, and collate them, we may find that the mortality in one year is 20 per cent. and in another 40 per cent. Not all of these cases are in private practice. It is also well known that in some epidemics nearly all cases recover, and in others there is great mortality. In order, therefore, that statistics should be worth anything they should be collected during one epidemic, under similar circumstances, and, if possible, by the same observer. Thus he might treat 150 cases of diphtheria with the antitoxin and 150 cases without and report the results. I may say, however, that all the statistics that have thus far come to my knowledge have invariably shown a reduced mortality with antitoxin compared with other cases treated without it.

Of course, the diphtheria antitoxin is not a specific treatment in the same way that vaccination is against smallpox. It does not destroy the bacillus of diphtheria, but it checks the course of the disease. Another fact is that the Klebs-Loeffler bacillus is very commonly present in the body, in the nose and throat, while every other symptom of diphtheria is absent, and it is just as much a mistake to class these cases as diphtheria as to consider the presence of diplococcus in the mouth as conclusive evidence of pneumonia, or tubercle bacilli in the air-passages as constituting a case of phthisis. It requires other symptoms of diphtheria, such as fever and sore-throat, than the mere presence of the diphtheria bacillus to constitute a case of diphtheria.

Immunization lasts only for a few days. In a hospital in Boston where diphtheria broke out all the inmates were immunized, and there was entire freedom from further cases for thirty days, but at the end of this time the cases began again to break out, and immunization was repeated and there was

again a freedom from new cases. The effects continue in some persons from fifteen to sixteen days, in others longer.

In the treatment of diphtheria it is to be acknowledged that the serum injections have not been uniformly successful, even in cases where the treatment began on the second or third day. The best results have been obtained where the ordinary remedies have been used in conjunction with the antitoxin serum. Just as in phthisis, creosote is used in addition to cod-liver oil and the usual remedies, so in diphtheria, in addition to the antitoxin, we use agents for cleansing the air-passages, reducing the fever, and attending to the general symptoms. With regard to the statistics of intubation and of tracheotomy, as far as I can find out, antitoxin does not reduce the necessity for either intubation or tracheotomy. Just as many cases require operation now as formerly was the case when antitoxin was not used. At the same time the results of operative interference conjoined with antitoxin are more successful than formerly. Thus, antitoxin serum does not dispense with the necessity for intubation or tracheotomy, but it improves the prognosis.

With regard to diphtheritic paralysis, it occurs just as frequently in those cases where the antitoxin is used as in others not so treated. At the same time the results are more favorable. With regard to the complications attributed to the injections, such as erythema, urticaria, arthritis, fever, etc., I have not been able to find any case in which the so-called complications have resulted in death. In the fatal case occurring in Brooklyn, after an injection, there was no explanation of the death. That these complications are annoying and troublesome there can be no question; some of them appear to be undoubtedly septic, but I have found no cases where this was the cause of death.

With regard to the appearance of albumin in the urine, it is to be remembered that albuminuria and nephritis are not synonymous terms. Very many cases of diphtheria have albuminuria; comparatively few have nephritis. In the cases which have died it appeared that the antitoxin rather increased the number of instances of renal complications.

DR. GEORGE A. MUEHLECK: Last November I had the privilege of reporting before the Surgical Section of the College of Physicians three cases of diphtheria successfully treated with antitoxin. Since then the serum was used in every case of diphtheria coming under my observation. My experience extends over 26 cases in all. Of these, 6 were laryngeal, purely; 3 were laryngeal and faucial; 3 were laryngeal, faucial, and nasal. Of the remaining 14, 8 were faucial and 6 nasal and faucial. In these 26 cases there were 3 deaths, a mortality of about 12 per cent.

The first fatal case was that of a little girl, two years old, with faucial and laryngeal diphtheria, following measles. On the third day of the disease 1000 antitoxin normals were injected; the child did well; was sitting up on the fourth day; membranes had disappeared, the voice had become clear, when, suddenly on the twelfth day, she became comatose, and died within three to four hours.

The second case was that of a little girl, four years of age, who came under my care on the seventh day of her disease. Her condition at that time was extremely precarious, the whole respiratory tract seemed involved. The

cervical glands were extensively infiltrated, the temperature subnormal, the urine very scanty, and containing large quantities of albumin and numerous casts. I injected 750 antitoxin normals of Schering's serum, but she died twelve hours later.

The third fatal case was that of a boy, one year old, who was comatose when I first saw him. Seven hundred and fifty antitoxin normals were injected, and death occurred a few hours later.

In all the other cases the injections were made within forty-eight hours of the onset. In five cases extensive erythema appeared after six to seven days. In no case did I observe any affection of the joints. Albumin in the urine was frequently noted in the more severe cases, but not more frequently than before the use of the serum. The temperature was very frequently reduced, generally within twenty-four hours after the injection, but in nearly all cases showed a tendency to rise again. This reduction of the temperature seemed to me to be much less pronounced when mixed infection existed, and generally in these cases a bacteriologic examination disclosed the presence of numerous streptococci, staphylococci, and other pathogenic organisms. The influence of the treatment upon the local manifestations in the pharynx generally became apparent within forty-eight hours. The membranes became pultaceous, and disappeared in five to eight days. The membranous exudations in the larynx were not, however, so promptly influenced, generally requiring from eight to fourteen days before all symptoms had disappeared. The stenosis, on the other hand, seemed to me to be very favorably influenced, so that even in those cases where intubation became necessary, the tube would either be coughed out, or could be taken out after four or five days. The general behavior, too, of these cases seemed to be more favorable, the depression usually following intubation after twelve to twenty-four hours, in which formerly so many children perished, seemed to me to be much less marked than before the use of the serum. The progressive emaciation which so frequently followed when the tube had to be kept *in situ* during a longer period was, of course, obviated. The local treatment consisted of the application of ice to the throat and the painting of the fauces, tonsils, and pharyngeal wall with a solution of mercury bichloride, 1:1000, twice or three times a day, thus obviating the necessity of overtaxing the already overburdened heart by the struggles to overcome the resistance of the child to too frequent applications—an advantage of no mean importance. The general treatment consisted of iron, general tonics, good food, and as favorable hygienic surroundings as possible. The erythematous eruptions noticed by me generally occurred about one week after the injection of the serum, disappearing in from six to seven days, without causing much discomfort, save a burning or itching sensation. The urine generally cleared up as convalescence progressed. The bacteriologic examinations were partly made by Dr. Ravenel, partly in my own laboratory, and partly by Dr. Bolton. These examinations often disclosed the presence of bacilli in the throat so long as two to three weeks after convalescence seemed to have been complete, thus demonstrating the necessity of strict isolation and thorough disinfection during a considerable time after apparent convalescence, whether serum had been used or not. About forty children in the families in which my cases occurred were immunized,

and not in a single instance was one of them attacked, although cultures taken from their throats frequently contained numerous Klebs-Loeffler bacilli. If I be permitted, from the study of my limited number of cases, to arrive at any conclusions, they would be as follows:

First. Antitoxic serum of diphtheria exerts a very marked influence upon the local manifestations of the disease, inasmuch as the membranes disappear sooner than under other forms of treatment. Intubated cases can, therefore, be extubated sooner than heretofore.

Second. Depression is markedly lessened.

Third. Temperature is favorably influenced where mixed infection is not too marked.

Fourth. The earlier in the attack the serum is injected, the more favorable is the prognosis.

Fifth. When the disease has lasted a number of days, and the toxins have already exerted their deleterious influence on the organs and upon the nervous system, antitoxin is as powerless to restore these parts as any other plan of treatment.

Sixth. Deleterious influence of the serum, in the vast majority of cases, is not observed; the most frequent manifestations being erythematous eruptions, which were, however, always temporary, and disappeared without serious results.

Seventh. It is possible to immunize healthy individuals temporarily by injecting the serum.

Eighth. The serum does not destroy the Klebs-Loeffler bacilli in the throat. They persist as long after convalescence as under other forms of treatment.

DR. LOUIS JURIST: My experience with antitoxin serum includes only half a dozen cases during the last year, occurring in my own practice or coming under my observation. I have come to the conclusion that if there is anything settled with regard to this treatment, it is this: if a case of diphtheria is held under observation until the fifth, sixth, or seventh day, and then antitoxin is resorted to, it will invariably result in failure. The first case I recall was one of this character where antitoxin was used on the ninth day, and the child died that night. And this is the invariable result where the treatment is delayed so long. I had another case in a family which had lost three children from diphtheria some years before, both intubation and tracheotomy having been unsuccessful. When I was called in a child of ten years was sick with mild diphtheria, and recovered with very little treatment. The next case in this family was one of laryngeal diphtheria in a child of seven years. The parents declined intubation or any operation, on account of their previous experience. I resorted to antitoxin, and injected one bottle. In about fifteen or twenty hours afterward the child had a strangling fit of coughing and expectorated a large mass of membrane which was an entire cast of the larynx. The child then went on to recovery without further incident. The family was immunized, and there were no more cases.

I am convinced that the diphtheria antitoxin is destined to speedy decline if exposed to the same experience as tracheotomy, which, by the general practitioner, is generally delayed until too late to do any good, and regarded as a last resort. Intubation is more successful because it is being employed

earlier, and the same will be true of antitoxin serum. I will say that if I had a case of diphtheria in my own family I would employ this treatment.

DR. I. N. SNIVELY: I have had five cases of diphtheria since July 1, 1895, all treated successfully by Mulford's antitoxin. The case Dr. Jurist referred to occurred in my practice one year ago. In that case I used antitoxin—Behring—on the tenth day of the disease. The patient was completely saturated by the poison of diphtheria, and died from paralysis of the heart. This case was not a fair test of the antitoxin, as it was used too late. Two days after this patient died I contracted the disease myself, probably from this case, although I had been treating diphtheria for several weeks and had ten or twelve cases in all at that time, with four deaths. I used antitoxin in none of this series of cases except the one referred to by Dr. Jurist, as the drug was very hard to secure at that time, and comparatively little was known of its value.

In my own case no antitoxin was used for the reasons already given. I was taken sick on September 26, 1894, and was disabled for five weeks. My constitutional symptoms were comparatively light and few in number; fever ranged about 100° to 101° F; pulse 90–95. The local symptoms were very severe: I can think of nothing to compare with the pain in the throat. We found it difficult to clear the throat of the membrane; even three weeks after the beginning of the disease large patches of membrane were seen on the tonsils and fauces; my treatment was iron, bitter tonics, and whiskey, and locally we applied peroxide of hydrogen in a much diluted solution, as the concentrated solution was too painful. I subsequently had paralysis of the faucial muscles.

In the five recent cases mentioned before as treated by antitoxin, I had the diagnosis confirmed by a bacteriological examination; these examinations were made in the Laboratory of Hygiene, Bureau of Health, of this city, Dr. Bolton, Director. In every case the drug was used early in the course of the disease, and the effect was most marked and satisfactory. The disease was cut short and the recovery of the patients was prompt, and no bad effects were noticed in any case. I examined the urine in all cases treated and found albumin in only one case, and in small quantities in this case; it soon disappeared from the urine on proper treatment. Thus, you see, I had five cases and no deaths. Several of the cases gave evidence of the severest forms of the disease.

DR. S. SOLIS-COHEN: The lecturer has used the name of my brother, Dr. J. Solis-Cohen, in connection with an antitoxin made in New York. I would explain that he has had nothing to do with its manufacture directly, but that he sent a horse to Dr. Briggs to be used in the early experiments when antitoxin serum was scarce and dear, and before any commercial houses or municipal authorities in this country had commenced its preparation. The serum thus obtained through Dr. Briggs, at Dr. Cohen's expense, is not for sale, but so long as the supply lasts it is at the service, free of charge, of any member of the Society, or other reputable physician, whose patients may be unable to pay for the commercial serum. It has been largely used at the Municipal Hospital and by Dr. Rosenthal, Dr. Muehleck, and others, with results fully equal to those gotten from the serum imported from Germany. My own personal experience with diphtheria antitoxin is limited; in fact,

but three cases, all of which recovered. Two were laryngeal and one was pharyngeal diphtheria; and intubation was necessary in one of the laryngeal cases. I agree very fully with Dr. Rosenthal and others, in the opinion that it is necessary to use the treatment early in order to get the best results, and that in complicated cases we must not always expect the best results. I would strongly indorse the remarks of Drs. Graham and Muehleck with regard to the necessity of disinfecting the throat, but I would also like to insist upon not only the uselessness, but the positive harmfulness of too many applications. The children should not be disturbed too often, and violence should never be used for fear of causing abrasions which would facilitate the absorption of the poison, and because the exhaustion of the struggle is likely to hasten death. Thus, on the one hand, the necessity of making thorough local applications is to be emphasized, but, on the other, equal stress is to be laid on the danger of making them too frequently; once or twice daily is often enough.

DR. EDWIN ROSENTHAL: I would only add to the discussion one remark, and that is that I think there is no necessity of sending abroad now for antitoxin, when serum of equal value can be obtained in this city. I have seen but two fatal cases in this method of treatment, and in both Behring's serum was employed. In all the cases in which Mulford's antitoxin was used under my observation the results were successful, as also all the cases I have seen treated with the serum from Dr. J. Solis-Cohen's horse have been successful. I am speaking only of what has come under my own observation, and not to condemn the imported serum. I merely wish to state that the results of the American preparation have been perfectly satisfactory in my hands, as well as in the hands of others.

With regard to the value of this method of treatment of diphtheria I can only say that my faith in it is such that if I were called to treat a case, and could not get the antitoxin, I should be very much at a loss indeed; for then I would have to contemplate what was before the sufferer—the days and nights of ceaseless vigil and work, and then the result always dubious. And with antitoxin: how the duration of the disease is shortened, how relief is quickly obtained, and the gratifying results. Again, where immunization is practised it takes away the dread of the disease from those in attendance, and the relief to the minds of such individuals cannot be estimated.

When intubation is practised the tube can be withdrawn in a much shorter time than without this treatment, and we can almost speak with certainty of the day when this is done. This is of great importance, especially when we are called into country districts or where the patient lives at a distance, because visits are necessary, and the sooner the case is over the better. I recollect one case in the practice of Dr. Frank T. Anderson, at Paschallville, where the tube was withdrawn and reinserted for twenty-eight days; this was during the time when antitoxin was unknown. The distance from my home was probably eight miles, and necessitated a number of visits. Since the antitoxin period I visited a case with Dr. Anderson in the same section of this city, and in three days my attention ceased. So in other cases; and for that reason I always reiterate, that in laryngeal diphtheria antitoxin is specifically indicated, and its marvellous value can here be proven.

